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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/637,302	HOOD ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-67* is/are pending in the application.

4a) Of the above claim(s) *7-13,17-40 and 42-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 6, 14-16 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed April 24, 2003 amending the title, amending claims 1-3, 5, 14, 15 and 41 and canceling claim 4 has been entered.

Claims 1-3 and 5-67 are pending. Claims 7-13, 17-40 and 42-67 are withdrawn.

Claims 1-3, 5, 6, 14-16 and 41 are under consideration.

Election/Restriction

Newly amended claim 1, with dependent claims 14-16, is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 1 encompasses the subject matter of elected Group I and the subject matter of non-elected Group II that are drawn to structurally and functionally different polypeptides (Office action mailed October 2, 2002, page 5). Therefore, where structural identity is required, such as for pharmaceutical effects or antibody reactivity the different proteins have different effects.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1 and 14-16 have only been examined with respect to the active Raf protein.

Claim Objections

Claims 1 and 14-16 are objected to under 37 CFR 1.75(d)(1) as being in improper form because the claim states an improper Markush group. Compounds included within a Markush group must (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility (See MPEP ° 803.02.) The current claims recite "active Raf protein" and "inactive Raf protein". The members of the Markush group, meet neither requirement, *supra*, because they represent structurally and functionally different polypeptides (Office action mailed October 2, 2002, page 5). Therefore, where structural identity is required, such as for pharmaceutical effects active Raf protein and inactive Raf protein have opposite effects and therefore, different utilities.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, with dependent claims 2, 3, 5, 6, 14-16, and claim 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 and claim 41 have been amended to recite an "isolated" Raf protein. The Examiner is unable to locate adequate support in the specification for such limitation. Thus there is no indication that a pharmaceutical composition comprising an isolated Raf protein (in opposite to a Raf protein expressed in a cell transformed with a polynucleotide encoding thereof) was within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Freed et al.

Freed et al. (US Patent 5,597,719) teach human Raf protein of SEQ ID NO:2 that is 100% identical to SEQ ID NO:2 of the instant invention and its functional fragments (columns 1-4, line 15). Said fragments include C-terminal kinase domain

303-648 and raf-CAAX (Figure 4; column 6; column 16, lines 55-65; column 27, lines 5-29). They teach expression of the full length Raf and its fragments and fusions in host cells (column 18). They further teach isolation of Raf proteins by immunoprecipitation using a Raf specific antibody (column 14, lines 42-49). A solution comprising an isolated Raf protein represents a pharmaceutical composition.

Statement of intended use in a pharmaceutical composition claim does not distinguish it over the prior art product, i.e. a pharmaceutical composition comprising Raf protein is the same product independent on its intended use.

Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Chow et al.

Chow et al. teach human Raf-1 protein and its N-terminal deletion mutants (abstract; page 14101, Fig.1). They teach expression of said proteins in host cells. Chow et al. teach the isolation of said proteins and measuring their kinase activity (page 14101, 1st column). A solution comprising an isolated Raf protein represents a pharmaceutical composition thereof.

Statement of intended use in a pharmaceutical composition claim does not distinguish it over the prior art product, i.e. a pharmaceutical composition comprising Raf protein is the same product independent on its intended use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5, 6, 14-16 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freed et al.

The teachings of Freed et al. are outlined above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce c-Raf protein (SEQ ID NO:2) or its fragments and fusions by the expression in a host cell and isolating them therefrom using a specific antibody as taught by Freed et al. A solution comprising an isolated c-Raf protein or its fragments and fusions represents a pharmaceutical composition. It would have been further obvious to one of ordinary skill in the art to produce an article of manufacture comprising a pharmaceutical composition comprising Raf protein of SEQ ID NO:2 or its

fragments and fusions and an identifying label optionally containing instructions for use.

Claim 41 is included in this 103 rejection because it would have been obvious to make different pharmaceutical compositions comprising Raf protein depending on the intended use.

One of ordinary skill in the art would have been motivated to produce such article in view of a great importance of Raf in various pathological processes known in the art and discussed by Freed et al.

Claims 1-3, 6, 14-16 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chow et al.

The teachings of Chow et al. are outlined above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce c-Raf protein (SEQ ID NO:2) or its fragments and fusions by the expression in a host cell and isolating them therefrom using a specific antibody as taught by Freed et al. A solution comprising an isolated c-Raf protein or its fragments and fusions represents a pharmaceutical composition. It would have been further obvious to one of ordinary skill in the art to produce an article comprising a pharmaceutical composition comprising Raf protein of SEQ ID NO:2 or its fragments and fusions and an identifying label optionally containing instructions for use.

Claim 41 is included in this 103 rejection because it would have been obvious to make different pharmaceutical compositions comprising Raf protein depending on the intended use.

One of ordinary skill in the art would have been motivated to produce such article in view of a great importance of Raf in various pathological processes known in the art and discussed by Chow et al.

Response to Arguments

Applicant's arguments filed April 24, 2003 have been fully considered but they are not persuasive.

Applicants argue that the claimed invention is distinguished from the prior art because they claim "a pharmaceutical composition comprising a protein, not an oligonucleotide" (Remarks, page 7, specifically line 16). This is not persuasive because the Skopinska-Rozewska et al. and Zhou et al. references teach transformed cells that express Raf proteins. As such they represent pharmaceutical compositions comprising Raf proteins.

Applicants further stress the fact that the cited references do not teach the use of Raf protein for stimulating angiogenesis (page 7, 1st and penultimate paragraphs; page 8 and page 9). This is not persuasive because of the following. The instant claims are drawn to a pharmaceutical composition or an article of manufacture comprising

thereof. The product, i.e. human Raf protein (SEQ ID NO:2), is known in the art. Its C-terminal fragment is known. Raf-caax of SEQ ID NO:7 is known. Preamble of intended use in a pharmaceutical composition claim in no way distinguishes it over the prior art product. It appears that Applicants consider the pending claims equal to method claims but they are not.

With regard to an article of manufacture, it comprises, in addition to a pharmaceutical composition, a label. It appears obvious to label chemical compounds, in the instant case a pharmaceutical composition comprising Raf protein. The examiner's position is that the words on the label are irrelevant since said words and the label itself can not be patented and can not impart the patentability to the product. Said words in no way can constitute a substitution for method steps.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

Elizabeth Slobodyansky, PhD
Primary Examiner

July 10, 2003